DISSERTATION ON

USEFULLNESS OF TRANEXAMIC ACID IN REDUCING POST OPERATIVE BLEEDING IN PATIENTS UNDERGOING CARDIAC SURGERY

submitted in partial fulfillment of requirements of

M.CH DEGREE EXAMINATION

BRANCH

CARDIO VASCULAR AND THORACIC SURGERY

MADRAS MEDICAL COLLEGE AND

RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL

CHENNAI – 600 003.

AUGUST 2014

CERTIFICATE

This is to certify that the dissertation entitled "**USEFULLNESS OF TRANEXAMIC ACID IN REDUCING POST OPERATIVE BLEEDING IN PATIENTS UNDERGOING CARDIAC SURGERY"** presented here is the original work done by **Dr.PREM ANAND.J,** in department of Cardio Thoracic Surgery, Rajiv Gandhi Government General Hospital. Madras Medical College, Chennai – 600 003, in partial fulfillment of the University rules and regulations for the award of Branch-I M.Ch Cardio Vascular and Thoracic Surgery Degree under our guidance and supervision during the academic period from January 2013 to December 2013.

Prof.R.VIMALA, M.D.,
Dean,
Rajiv Gandhi Government
General Hospital. Madras Medical
College, Chennai – 600 003

Prof.K.RAJA VENKTAESH, MS.M.Ch
Professor and HOD,
Department of CVTS,
MMC/RGGGH,
Chennai

DECLARATION

I Dr.PREM ANAND.J hereby solemnly declare that this dissertation titled "**USEFULLNESS OF TRANEXAMIC ACID IN REDUCING POST OPERATIVE BLEEDING IN PATIENTS UNDERGOING CARDIAC SURGERY"** was done by me in the Department of Cardio Thoracic Surgery, Rajiv Gandhi Government General Hospital. Madras Medical College, Chennai – 600 003, during the period form January 2013 to December 2013 under the guidance and supervision of **Prof.Dr.K.RAJA VENKATESH,M.S.M.Ch.,** This dissertation is submitted to the Tamil Dr.M.G.R.Medical University towards the partial fulfillment of requirement for the award of M.Ch Degree in Cardio Thoracic Surgery.

Signature of Candidate

Place :

Date :

ACKNOWLEDGEMENT

Foremost , I would like to thank **Prof. R. vimala M D,** our dean, Madras medical college, for allowing me to conduct my thesis in the department of cardiothoracic surgery.

And my sincere thanks to my chief and head of the department **Prof.K. RAJA VENKATESH,** a teacher truly by example, for his encouragement ,guidance and beyond a fraternity, his capability of care towards post graduates pars paternal care.

I thank my professors **Dr.KASINATHAN, Dr. R.K.SASANKH, Dr. GANESAN, Dr.MARIAPPAN and Dr. AMIRTHARAJ.**

I am thankful to my assistant professors who have guided me through everything and put forth their efforts to make this study complete.

I thank my seniors ,my colleagues and my juniors for their help support and encouragement.

And I am eternally grateful to **Prof. Dr.N .NAGARAJAN** for treating us like his own children. A man who really stands tall.

I thank **Dr. ARUN KUMAR…AK** two as fondly referred to, for being the man he is.

I thank all the nursing staff and theatre staff for their support.

And in the process of making me eligible to be among the elite of the fraternity,it's my honour and singular pleasure to thank my family for the support extended.

My uncle **Mr.A.M MARIASELVAM,** who is a legend by his way of living, has extended his support to the extremes of all level always inspired me to **…..DREAM BEYOND….**

My aunt **Mrs.KANCHANA MALA** ,for not just believing in me, but for her strength of being the **BANYAN** among the times of crisis,taking up all our stress on her shoulders.

My dad **JOHN .C,** to simply say, is a human by form, and divine by existence….he is my guide, inspiration and MY GOD at all times.

My mom **D.ANANDA MARY**, for her extra ordinary vision, strength and resolve, her traits ain't human,definitely more than divine. The god of gods bestowed with the power to turn a desert into eden.

Last and importantantly, the core of my life, to my beautiful wife **M.S.SANGEETHA**, for simply bearing with all my idiosyncracies and for her truly unconditional love.

And to my kids bonje and Claudia for giving me a reason to celebrate life.

INDEX

INTRODUCTION

Cardiac surgery has grown up with regard to technical advances..and major cardiac anomalies are repaired ,majorly aided and eased with the advent of cardio pulmonary by pass…

Extra corporeal circulation has made it extremely safe, in providing perfusion to the heart, rendering the heart more accessible and amenable for complicated procedures.

But the use of cardio pulmonary by pass has not been free from adverse effects …there is a hoard of changes that happen at the bio molecular lever which triggers off, a whole body inflammatory response…

The commonest function to be hampered is easily the physiology of circulation. There is significant amount of disruption in the normal coagulation system ,leading to trivial to significant blood loss..

The reason for this altercation would be in multitude, and to name a few…

- ❖ Fall in the quantity of platelets
- ❖ Decrease in the factors that aid in clotting

All this is possibly due to hem dilution…

Contact with the external circuit is another possible factor that can add to the woes.

After receiving the patient in post operative room, if there is significant or obscene bleeding, it possibly is due to a surgical cause,whereas if there is a steady rise in drains with no sudden hemodynamic instability associated with deranged clotting time,bleeding time or platelet levels, then it could be termed as medical bleed…

Medical bleeding, once it has been ascertained,can be rectified by various measures....compensating the loss with blood and blood products, protamine to neutralize heparin and administration of anti fibrinolytics like tranexamic acid..

The usage of blood and products is not safe in entirety,and can cause a mixture of problems adding on to the woes of the patient and the managing surgeon…

The efficiency of tranexamic acid in controlling post operative has been elaborately studied and various dosing regimens have been suggested… but there is no fixed dosing till date..in cardiac surgery..

We decided to fix up a dosage ,and check for the efficacy of this drug in reducing the immediate medical bleed in patients undergoing cardiac surgery in Rajiv Gandhi government general hospital.

AIM OF THE STUDY

The study was designed with the primary AIM of evaluating the effect of tranexamic acid in reducing the bleeding tendency in immediate post operative period for patients who have undergone cardiac sugery .

To evaluate whether tranexamic acid reduces the need for red cell transfusions. To understand the occurrence of post operative thrombo embolic events.

REVIEW OF LITERATURE

The advent of cardio pulmonary by pass has made cardiac surgery a relatively safer modality. The history of it's evolution is too elaborate and no one person could solely be identified for the clinical use.

John gibbon is one of the big names in pioneering cardio pulmonary by pass. In late 1930 s he was instrumental in advancing the application of that thought to clinical use.

Inspite of lack of support, his perseverance finally reaped benefits and he did his first successful cardiac surgery on CPB in 1953..since then CPB has evolved and come a long way in aiding cardiac surgery.

The other big names would be Dennis , Richard varco, Viking bjork, C.Walton lillehei and John kirklin.. The use of CPB coupled with oxygenator was first used in 1955, march 22 at mayo hospital, ant the surgery was repair of a ventriculo septal defect.

FEATURES OF CARDIO PULMONARY BY PASS

The systemic venous return to the heart is diverted to the pump oxygenator, and then returned via arterial lines to the systemic arterial circulation.. this artificial state of maintaining perfusion incites lot of physiologic process…a few to mention would be..

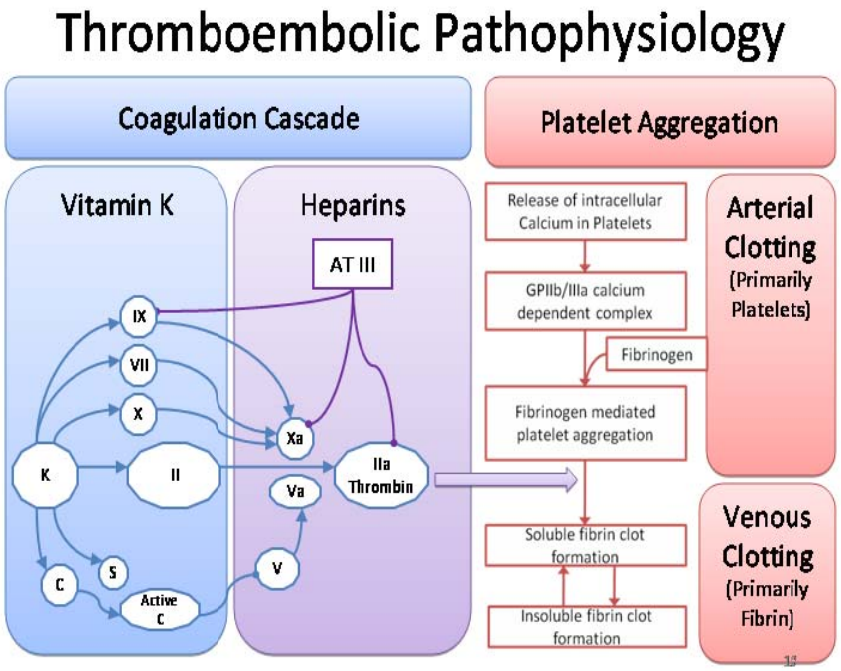
Humoral and cellular components of defense and inflammatory responses are usually altered.

The pressure gradients in systemic and pulmonary venous and arterial systems are manipulated.

Another system would be that of the physiology of coagulation cascade…that seems to take the brunt of all..with derangements in platelet functions ,decrease in clotting factors ,fall in haematocrit.

There are multiple other molecular level changes, oxygen consumption, mixed venous oxygen saturation, lactic acidosis ,regional and end organ tissue perfusion.

The physiology of normal coagulation cascade can be best illustrated .\\\\\\



Just before establishing cardiopulmonary by pass , the patient is anticoagulated generally to avoid thrombosis complicating the circuit.

The anticoagulant that is commonly used is HEPARIN, usually given at a dose of three to four milligram per kilogram of body weight. It belongs to a group of low molecular weight glycosaminoglycans and has a molecular weight ranging from Three thousand to ten thousand .

The mechanism of action is by producing a antithrombin 3 a like effect..and heparin is usually neutralized with protamine sulphate.

How ever there could be significant post operative medical bleed because of heparin re bound, which is attributed to either re circulation of heparin from tissue bound stores,or because of dissociation of heparin protamine complexes or because of shorter protamine half life time or may be a combination of all these factors.

Platelet activation during CPB has always been extensively studied and been attributed to be a major reason in causing post operative bleed.

It has been shown in vitro studies that there is quantitative decrease in platelet strength. There is a decrease of platelets by about sixty percent within two minutes of commencing CPB and a significant reduction by eighty percent within eight minutes of CPB and can remain so for about twenty four hours.

Platelet aggregates have been visualized in retinal arterioles even days after CPB..Platelet functions usually reverses to normalcy within three days after CPB.

Membrane oxygenator seems to be playing a crucial role in affecting the platelet functions. Oxygenators made of silicon rubber causes lesser platelet damage than bubble oxygenators.

Aprotinin has been proven to have reduce the platelet abnormalities, but has lost it's popularity in view of safety concerns.

Activation of coagulation cascade seems to be an important concern in going on CPB ,cause if the patient were not to be heparinised then almost immediately the respose would be massive thrombo embolism leading to pump failure, such would be the response of the activation..

This kind of activation is triggered by direct CONTACT, INTRINSIC and EXTRINSIC mechanism . This response is blunted by heparinising the patient. And even after heparinising ,there could be some amount of activation and fibrin formation,which has been attributed to post operative bleeding. This is possibly because most of the soluble clotting factors are reduced in quantity by the end of CPB.

It has been presumed that one of the important reasons for post operative bleeding was platelet dysfunction, recent studies have shown that activation of fibrinolytic cascade is also an added factor. Normally present in active plasminogen is converted to plasmin to cause degradation of fibrin products. The effect of plasmin on bleeding is proved by the fact that use of aprotinin reduces post operative bleeding. Aprotinin is a plasminogen inhibitor.

Hypothermia is another factor that could possibly aggravate post operative bleeding by causing platelet dysfunction.Thus it is important to have adequate rewarming on CPB. The use of platelet transfusion has been helpful.

Even the increased circulation of catecholamines can cause platlet dysfunction. The clot remodellin properties are reduced on activation of fibrinolytic cascade.

The response to CPB on coagulation cascade ,depends and varies from individual people..some blunted , some extremely sensitive to even minor stimuli.

Post operative bleeding usually is a major concern and might warrant re operation to avoid cardiac tamponade. Recognition of the cause of bleeding is crucial. Surgical causes is ruled out.Increasing drains with evidence of tamponade , points to a surgical cause usually.

Medical bleed is usually lesser but regular and can be predicted with associated abnormalities in bleeding time and clotting time and reverted with pharmacological support.

The etiology in post operative bleeding can listed as….

- Increased lysis of fibrin.
- Heparin overdosing.
- Protamine excess

- Decrease in clotting factors.
- Fragile clots vulnerable for fragmentation.
- Reduced platelet counts.
- Drug induced thrombocytopenia.
- In appropriate response of aggregation to mediators.
- Selective decrease in younger platelets.
- Fragmenting platelets.
- Plasmin mediated platelet dysfunction.
- Impaired clot re modeling mechanism.
- Haematological factors involved in CPB
- Kallikrein
- High molecular weight kallikrein
- Thrombin
- Plasminogen to plasmin
- Thrombexane two
- Serotonin
- Oxygen free radicals
- Tissue plasminogen activator
- Cytokines
- Complement 3a ,
- Complement 5a,

- Complement 5b-9.
- Adenosine diphosphate.
- The clinching of medical bleeding in post operative scenario is greatly facilitated with coagulation testing.
- The set up is complete with a centralized coagulation testing.
- The few commonly done tests are..
- Prothrombin time.
- Activated partial thromboplastin time.
- Clotting time
- d-Dimer
- Fibrin degradation products
- Platelet count
- Platelet aggregometry
- Ecarin clotting time

Prothrombin time ..a test wherein it involves incubated plasma,where the calcium is complexed previously with citrate ,so as to prevent activation of coagulation.

The incubated plasma is treated with thromboplastin,and since it comes with it's own phospholipid and tissue factor , the sample if it

contains adequate factor seven and factors involved in common pathway, the sample will gel faster in about twelve seconds.

The international normalized ratio allows comparison of prothrombin time with different commercial reagents.

The principle of aPTT is incubation of the plasma sample with thromboplastin without the tissue extract , so it has to clot with surface activation only. There are a lot of surface activation agents like silica, kaolin celite..etc…

Heparin usually alters aptt , but in large doses can alter prothrombin time.

The coagulation tests are usually done bedside or wherever the results can be available sooner so as to increase the rapidity with which a diagnosis can be made, because timely intervention is crucial in cardiac surgery.

Prompt intervention often saves lives.

There are lot of products available to enhance prompt lab evaluation with a drop of blood,they all work on different principles like magnetic rotation that ceases, optical interference ,electro mechanical disruption and clot formation with retraction.

Hypothermia ,hemo dilution, decreased platelet count and protamine excess can all derange or increase activated thromboplastin time.

Hence it is vital to adequately rewarm on CPB ,monitor heparin levels, titrate protamine appropriately only.hemodilution can be avoided with priming volume additives.

Even the best of precautions ,can never render a hassle free post operative period. Un explained bleeding remains one of the entity of what is termed as RESPONSE VARIABLES.

Recent advances in testing, advances in molecular biology, technical progress have all given us an excellent armamatorium in fighting cardiac diseases.

The pharmacological assistance has benefited innumerably.

The common drugs that have been deployed in combating post operative bleeding are..

Aprotonin

- Aminocaproic acid
- Protamine
- Tranexamic acid
- Vitamin k

Aminocaproic acid and tranexamic acid belong to the group of lysine analogs. The mechanism of action is that these drugs competitively binds to lysine binding sites of plasminogen/plasmin and thus prevents de gradation of fibrin or fibrinogen.

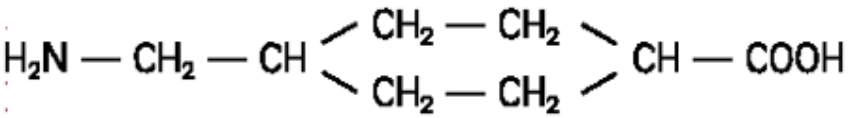
Tranexamic acid is a water soluble lysine analog..onset of action rapid by intravenous route. The biological half life is two to three hours and the drug is totally cleared by renal route..nearly 60% of the drug is excreted by renal system at three to four hours and about 90% in about twenty four hours.

There has varied dosing protocols and regimens. No specific benefit pattern fixed as of now. One popular trial had tranexamic acid given in doses of 10 to 15 milligram per kilogram of body weight.

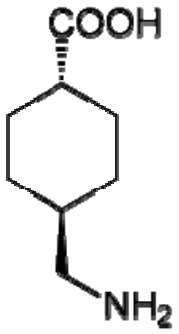
The adverse effects of tranexamic acid are lesser morbid and organ toxicity has rarely happened. Use of tranexamic acid has considerably reduced post operative bleed in patients known to have a higher propensity of bleeding.

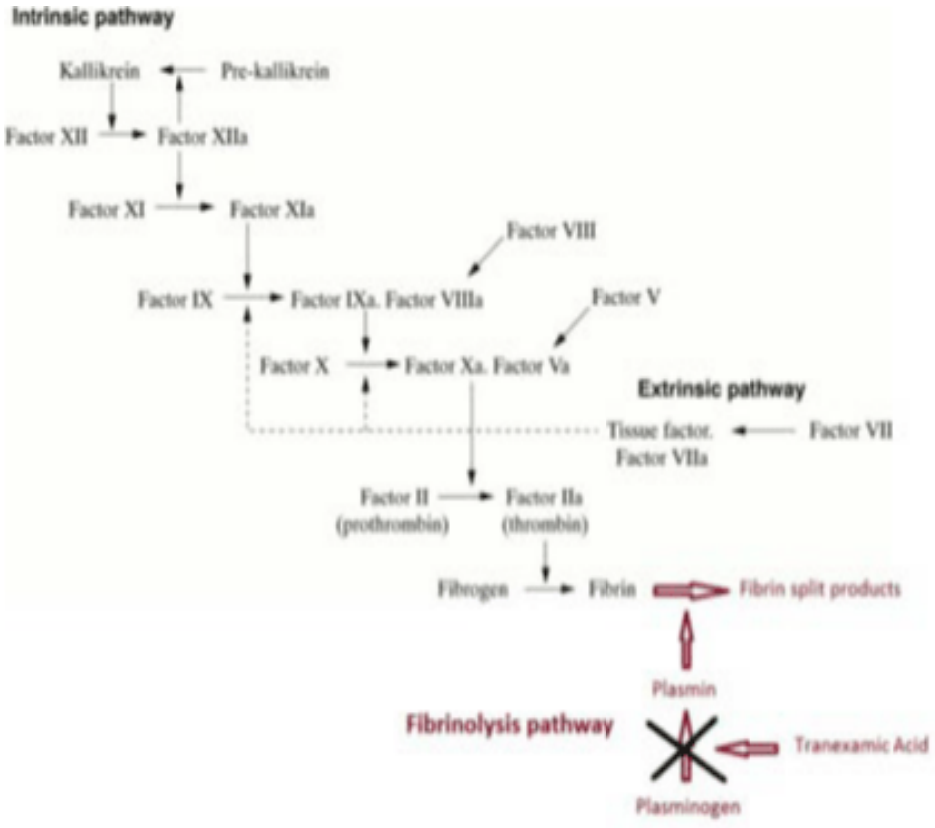
Based on the scenarios, the benefit varies.patients having long pump runs, lower haematocrit, body weight less than forty kilograms would benefit more with tranexamic acid.

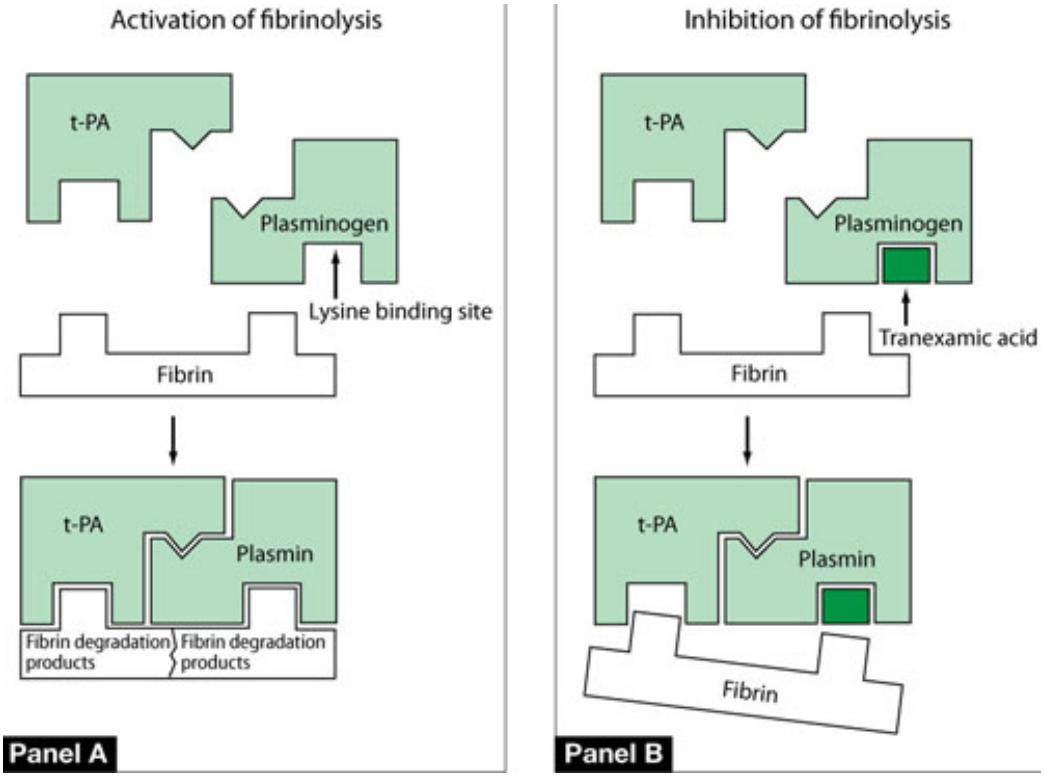
Chemical formula of tranexamic acid.



Trans 4 –cyclohexane carboxylic acid.


COOH
NH2


Intrinsic pathway
Kallikrein
Pre-kallikrein
Factor XII
Factor XIIa
Factor XI
Factor XIa
Factor VIII
Factor IX
Factor IXa. Factor VIIIa
Factor V
Factor X
Factor Xa. Factor Va
Extrinsic pathway
Tissue factor. Factor VIIa
Factor VII
Factor II (prothrombin)
Factor IIa (thrombin)
Fibrogen
Fibrin
Fibrin split products
Plasmin
Fibrinolysis pathway
Tranexamic Acid
Plasminogen


Activation of fibrinolysis
t-PA
Plasminogen
Lysine binding site
Fibrin
t-PA
Plasmin
Fibrin degradation products
Fibrin degradation products
Panel A
Inhibition of fibrinolysis
t-PA
Plasminogen
Tranexamic acid
Fibrin
t-PA
Plasmin
Fibrin
Panel B

MATERIAL AND METHODS

This study, designed to be prospective and randomized was undertaken as an observational evaluation on the topic of usefulness of tranexamic acid in reducing post operative bleed in patients undergoing cardiac surgery.

This study was conducted in the department of cardio thoracic surgery at Rajiv Gandhi government general hospital, Chennai.

This study design was for a year , 2013, and we used a descriptive analytical method.

INCLUSION CRITERIA

All patients undergoing open cardiac surgery procedures involving cardiopulmonary by pass.

EXCLUSION CRITERIA

- Patients with pre existing evidence of of coagulopathy.
- Patients with hepatic dysfunction
- Patients with renal dysfunction

- Off pump cardiac sugery cases

METHODOLOGY

Relevant information were documented in a specially designed proforma.

Meticulous clinical examination preceded by detailed history, using pre framed questions.

Sixty patients undergoing cardiac surgeries were randomized into a group of two, thirty each. One group of thirty patients would receive tranexamic acid , loading dose of 15 milligram per kilogram of body weight , five minutes before skin incision and one more similar dose after weaning from CPB. The other group would not receive tranexamic acid.

Assessment of efficacy obtained by evaluating post operative data.

Patients were received in post operative room and monitored. Routine blood investigations sent on arrival..chest drains were documented one hourly.clinical evidence for generalized medical bleed looked out for.red cell transfusion decided on appropriate indications

only.all this data was recorded and analysis drawn and conclusions made.

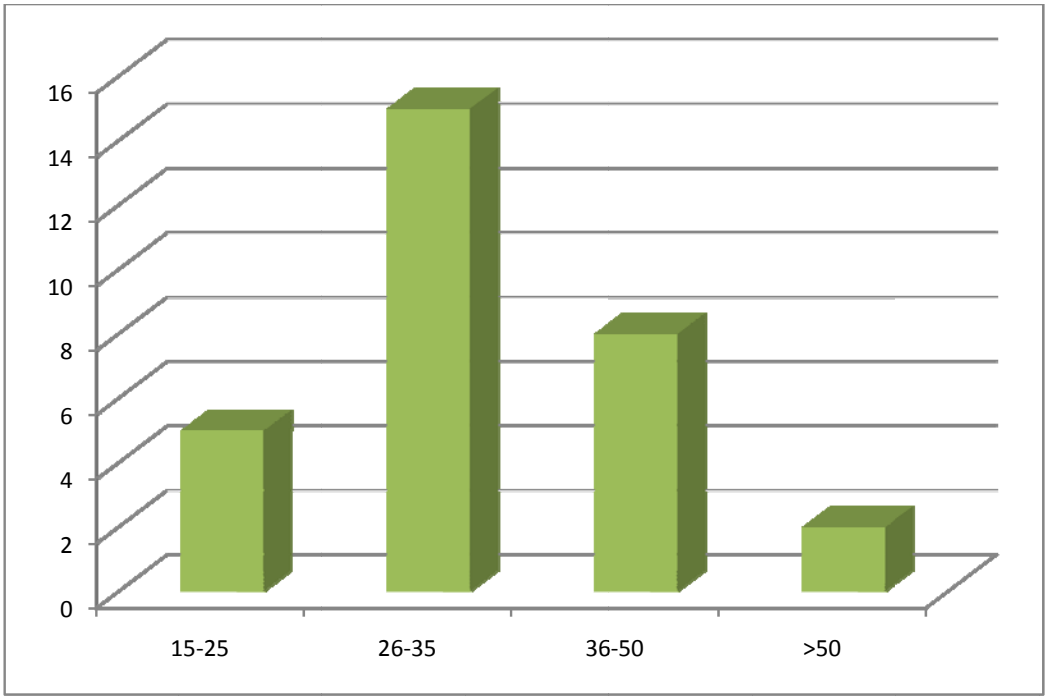
The patients were followed up during their hospital stay to record any events of thrombo embolism.

Ethical committee clearance was obtained and all procedures were performed without any ethical breach. The patient and their relatives were kept well informed about the procedure.

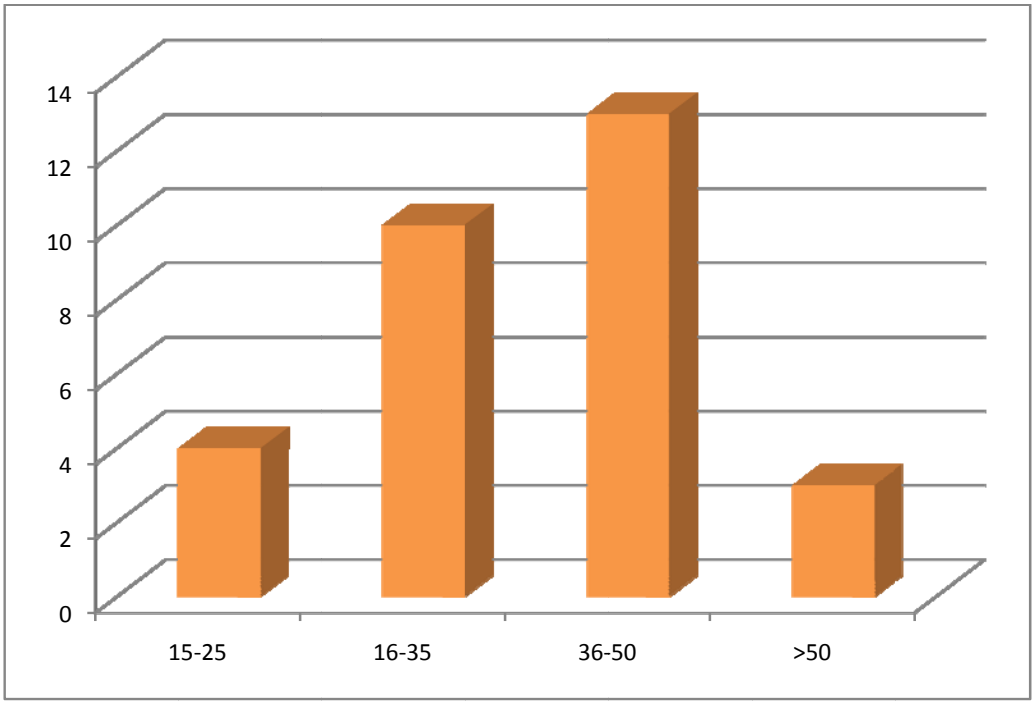
OBSERVATION

OBSERVATION.

EPIDEMIOLOGICAL DATA

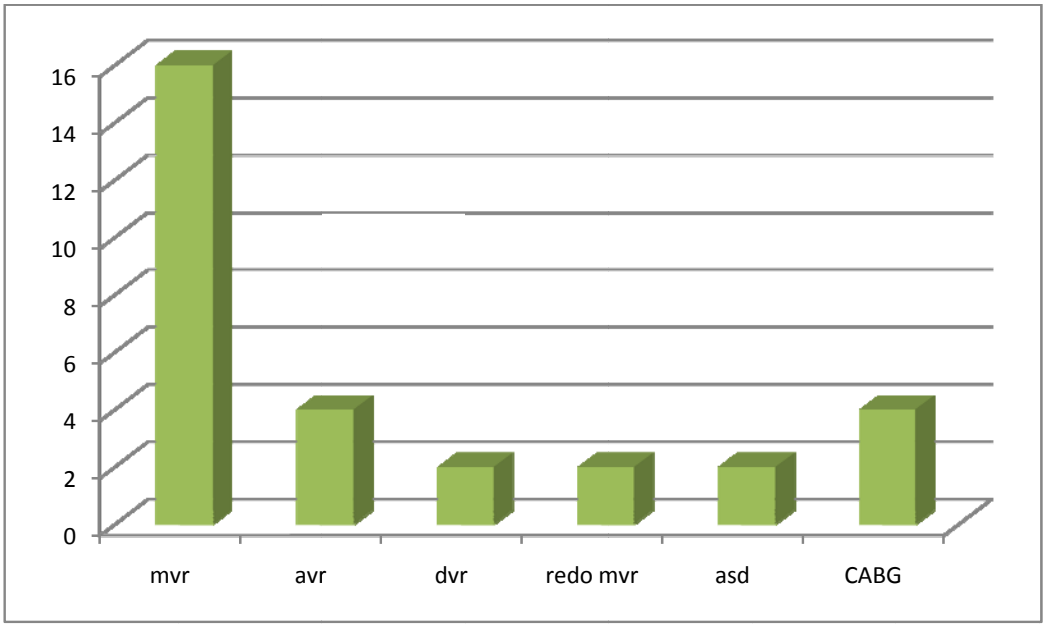


Sex distribution among patients who received tranexamic acid.



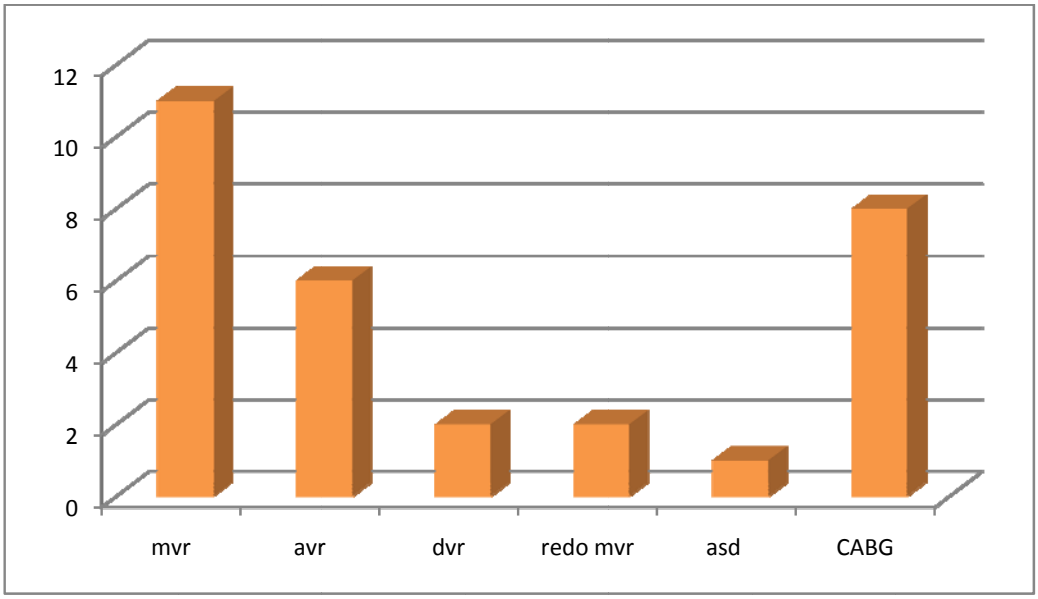
Sex distribution among patients who did not receive tranexamic acid

Pathology involved in tranexamic group.

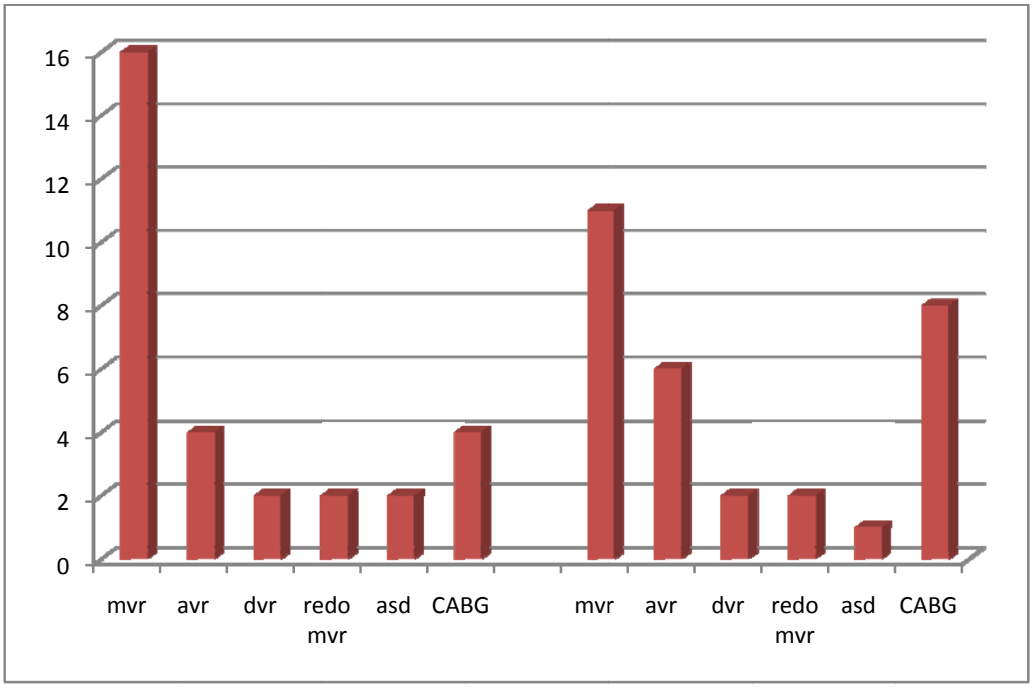


With a clear higher involvement of mitral valve disease.

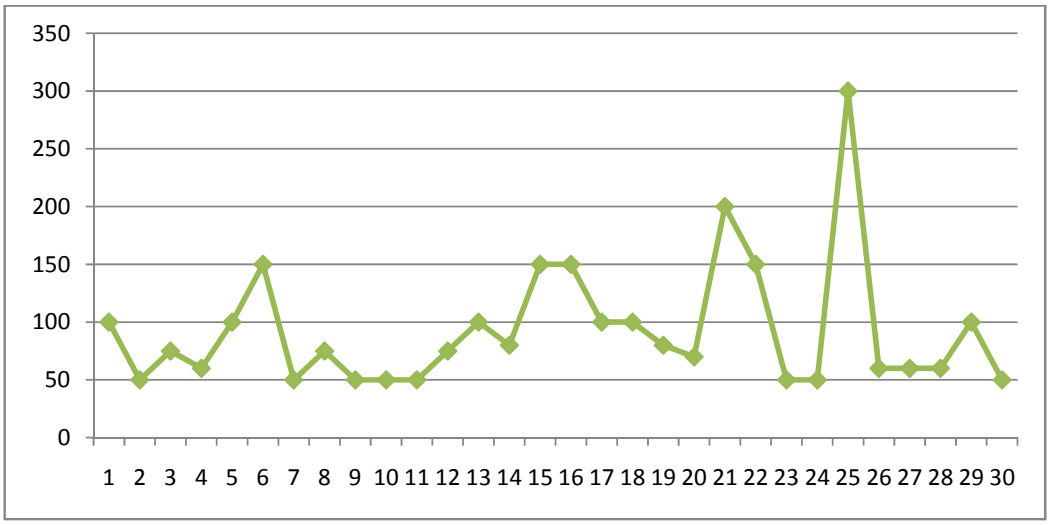
Pathology in the neutral group .



Pathology in 1) tranexamic group and 2) neutral group.



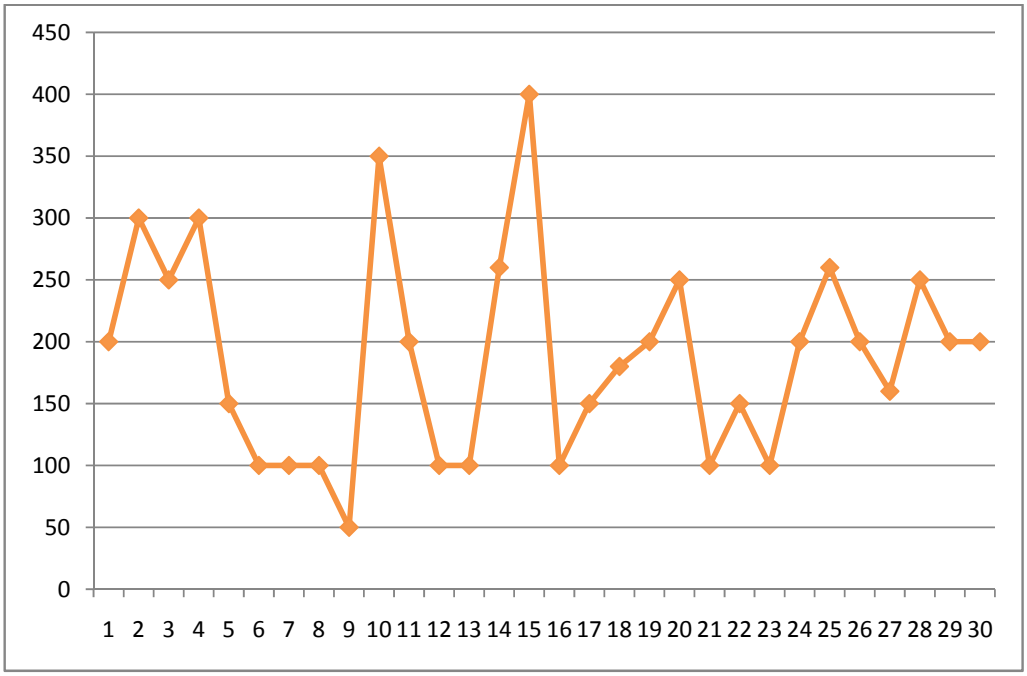
Drain trend in tranexamic group. Expressed in milliliter over first six hours.



Post op drain…mean 120 ml over six hours..std deviation…5.781.

P – value.....0.256

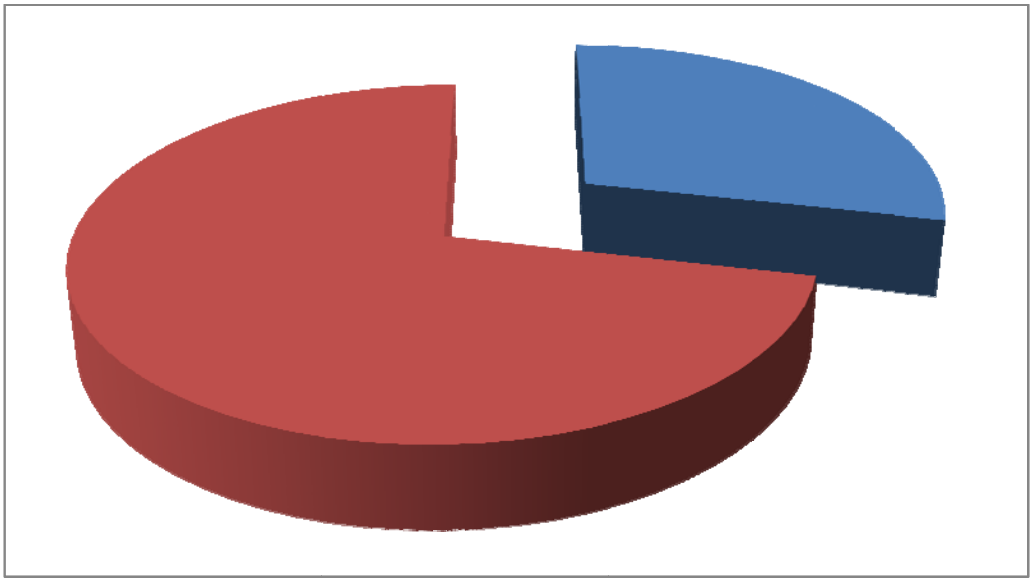
Drain trend in neutral group…blood loss expressed in millilitre for the first six hours.


450
400
350
300
250
200
150
100
50
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30

Post op drain at six hours..average..250 ml..std deviation..5.931

P – value 0.421..

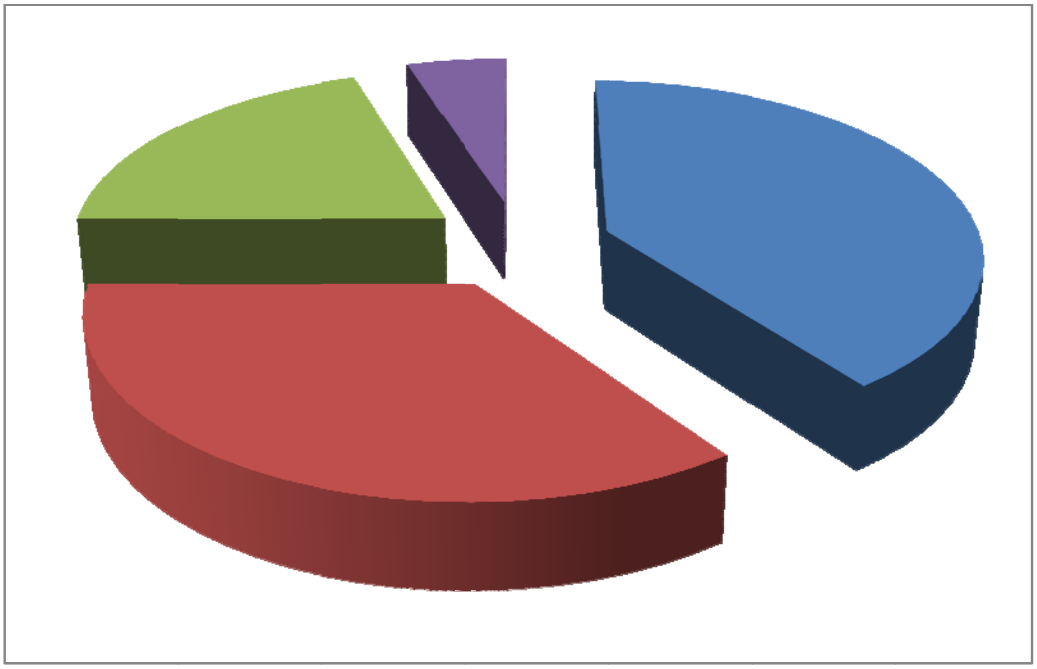
Packed cell transfusion in tranexamic acid group.



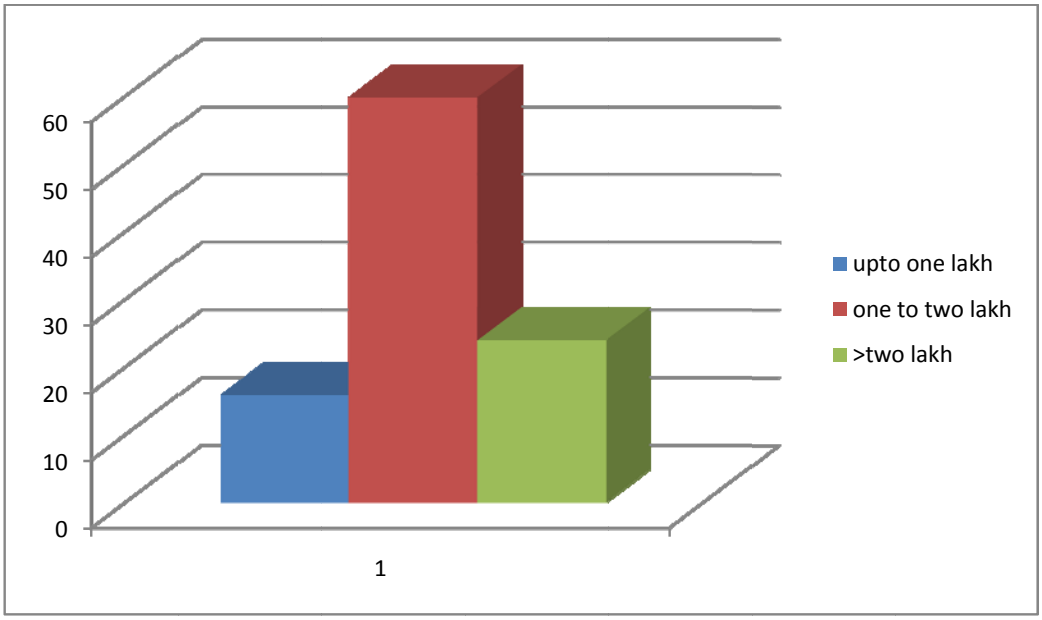
The blue area represents the fraction of patients who received one unit of packed cells…..40%

The other fraction represents the percentage of people who did not receive transfusion……60%

Packed cell transfusion in neutral group.



- The marroon represents 40% who received one unit of packed cell.
- The blue represents the 35% who received two units of packed cell.
- The green represents 20% who received three units of packed cells.
- The purple represents 5% who did not receive transfusion.
- Platelet count in tranexamic acid group in immediate post op.

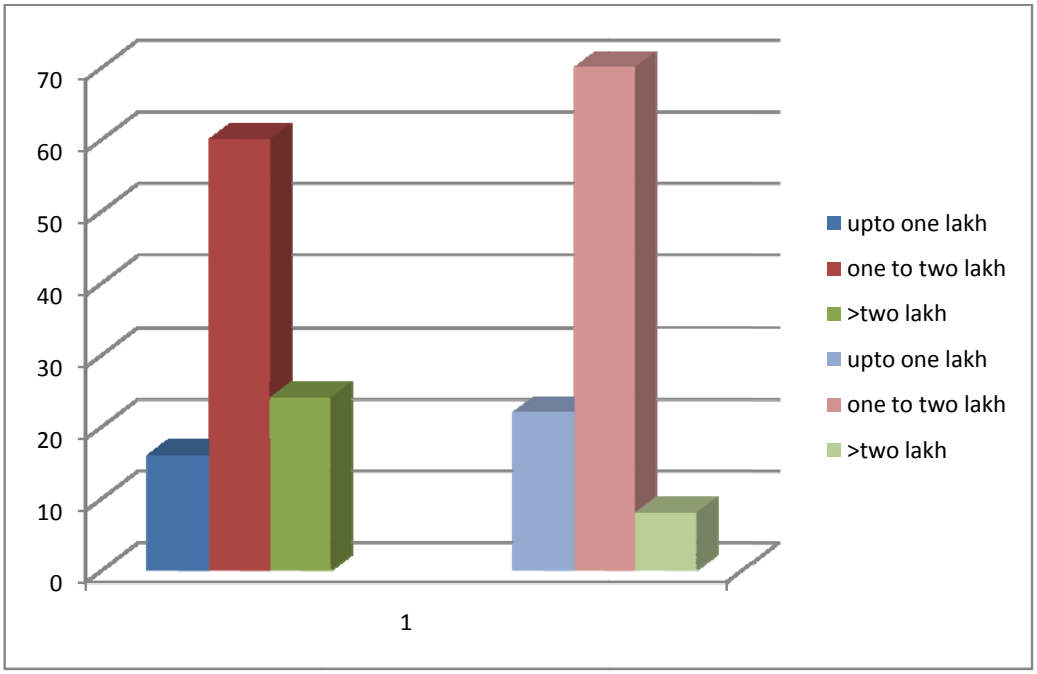

60
50
40
30
20
10
0
1
upto one lakh
one to two lakh
>two lakh

Y axis is in percentage of the patients.

Mean 1.25 lakhs. std deviation….6.338

P value ….0.587

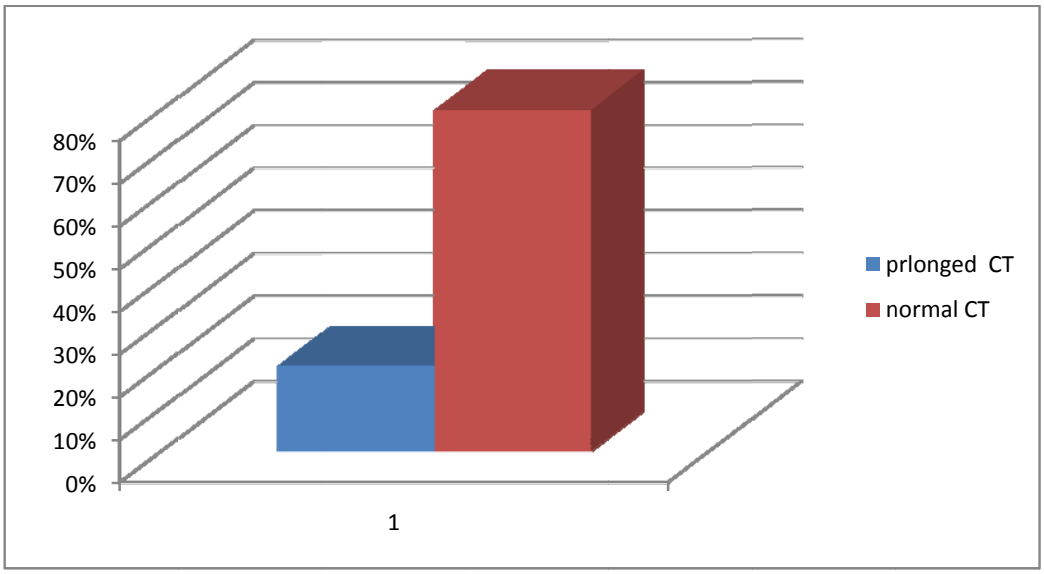
Platelets in immediate post op…in both groups.


70
60
50
40
30
20
10
0
1
upto one lakh
one to two lakh
>two lakh
upto one lakh
one to two lakh
>two lakh

The darker colour illustration is the tranexamic acid group, and the lighter colour represents the neutral group.

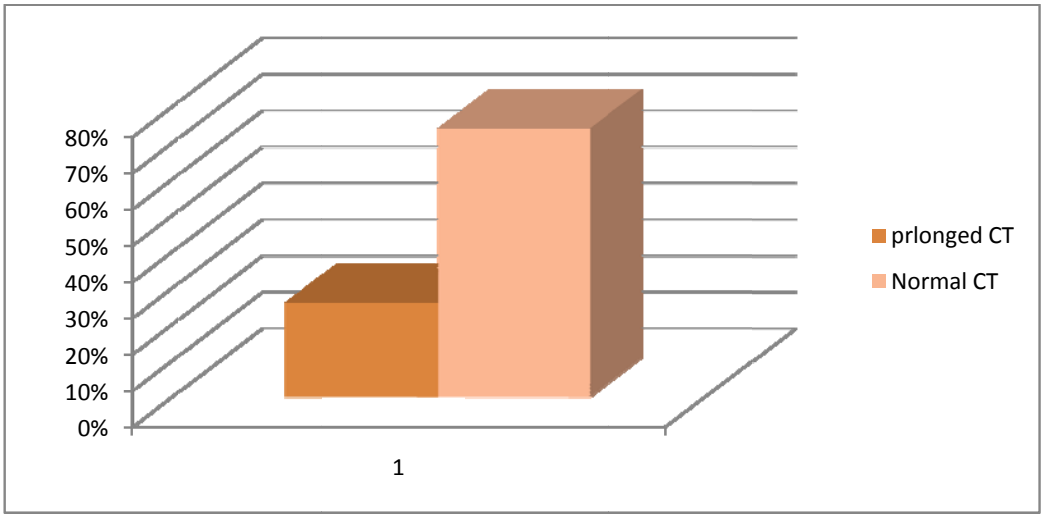
Mean ..1.1 lakh.. std deviation..20.57 .p value..6.840

Clotting time in tranexamic acid group.



Mean 6 mts…std deviation…4.620 p value…0.27

Clotting time in neutral group.



Pearson chi square test..0.039

P value…..0.744

DISCUSSION

This study was designed as a prospective and randomized study. This study was carried out in the department of cardiothoracic surgery, Rajiv Gandhi government general hospital in the year 2013.

The study included sixty patients undergoing cardiac surgeries in our department..they were randomized into a group of two, one group of patients received tranexamic acid at a dose of fifteen mg per kg body weight of the patient…one loading dosefive min before skin incision and one on weaning patient fom CPB..the other group did not recieve tranexamic acid.

The patients were operated by single team of doctors, follow up charted meticulously,recorded data converted into analytical data with the help of a statistician.

The patients had their routine follow up..no intervention was made specially. Clinical signs for medical bleed was carefully monitored. Drain levels documented.transfusions of packed cell decided based on haematocrit. There was no patient in either group who had to been re operated.

The drain trends were definitely higher in the group that did not receive tranexamic acid…this group was always referred to as the neutral group.

The patients had their routine blood investigations done at immediate post operative period.the neutral group did not receive any tranexamic acid at induction nor on weaning on CPB.

The beneficial effects were obvious with tranexamic acid group in the immediate post op.

The age distribution was almost similar to both groups..the young adult population seemed to dominate in both groups,underlining the higher incidence of rheumatic heart disease in that group.

The younger adult population makin upto fifty percent in tranexamic group and forty five percent in neutral group. And among the distribution of the pathology of heart diseases,mitral valve replacement was on top in both groups with 52% in tranexamic acid group and 42 % in neutral group, and CABG was more in neutral group, 24%.

The drain levels in tranexamic acid was an average of 100 ml over first six hours as compared to 250 ml of neutral group,the difference is striking,although the p value is not significant, the trend definitely points to the use of tranexamic acid in reducing post operative bleed.

The drain levels at twelve hours of post op period in both the groups are not too different,with an average of 100 ml and 150 ml in tranexamic and neutral group respectively. The drain levels at twent four hours remained almost similar ,averaging 50 and 100 ml respectively. The benefits of tranexamic acid in reducing post operative bleed is obvious, yet the benefits after twent four hours were not very obvious.

The drain levels there after were not taken into account, but no patient in either group had any alarming bleed.

The coagulation tests done on either group showed mild beneficial trends towards tranexamic acid.

There was a minimal difference in clotting time, with both groups having 65 to 68% of patients with normal clotting time. And so was the results with the platelet counts with no gross disparity between the groups.

The need for packed cell transfusion was only one unit in 45% and the remainder was not transfused in tranexamic acid group.

About 40% were transfused with one unit ,35% with two units, 20% with three units in the neutral group.

This reflects the obvious trend of increased need of red cell transfusion in the neutral group.

The platelet transfusions were given at eight hours or later only if there was a rebound bleed.

About four units transfused ,if required.there was no difference in platelets that was transfused, between the groups.

RESULTS

The observation and the analytical data from this prospective ,randomized study yielded the following results.

- In this study, either groups had a preponderance of young adult population. The age group of 25 to 36 were about 50% and 45% in tranexamic and neutral group.

- Mitral valve replacement was among the highest in both groups with close to 50 and 42% in tranexamic and neutral group.

- The mean post operative drain at six hours were 120 ml and 250 ml in tranexamic acid and neutral group, higher drain tendencies were reported in the neutral group.th p value was 0.27 not very significant, yet the trend reflects in favour of tranexamic acid.

- The need for red cell transfusion or packed cells were, only 45% required one unit of packed cell, in tranexamic acid group.

- The need for packed cell transfusion in neutral group was like, 40% required one unit, 35% required two units, and 20% required three and more, with 5% not requiring transfusion..

  \

- The clotting time tests were almost similar with not much of disparity, but a smaller trend of benefit in tranexamic acid group, which had 20% of prolonged clotting time, six percent lesser than the tranexamic acid group.

- The platelet counts too, showed a benefit trend towards tranexamic acid group.th p value was not significant though, with 0.587

- There were three mortality in each group, totaling six..and all the mortality were not related to the drug..the cause of death was low cardiac out put syndrome.

- There were no incidence of re operation due to bleeding in either groups.

CONCLUSION

- In this study , we come to the conclusion that using tranexamic acid reduces immediate post operative bleeding and significantly reduces the morbitity of the patient. However there is not much benefit in post operative period beyond twenty four hours.

- The need for packed cell transfusion also is significantly lesser with the tranexamic acid group.

- The abnormalities in clotting time and and platelets were almost similar with no statistical significance in either group,but showing marginal beneficial trend in tranexamic acid group.

- Tranexamic acid has been an efficient , cost effective and simple way in controlling post operative bleed in patients undergoing cardiac surgery.

BIBLIOGRAPHY

1) Murphy G J , mangon et al.. effects of tranexamic acid with cell saving measures in cardiac surgery. Journal of cardiothoracic surgery….2006; 132:475-80

2) Karski J M et al.. Effects of tranexamic acid in cardiac surgery in three different dosing regimens. Journal of cardiothoracic and vascular anaesthesia..2001;187:245-60

3) Reza jalaeian Tranexamic acid reduces blood loss in off pump CABG. Journal of cardiothoracic and vascular anaesthesia.vol .23 jun 2009

4) Bill I wong et al.. Effects of tranexamic acid in cardiac surgeries.Annals of thoracic surgery..vol ..69 issue 3

5) Blahut b harringer w, Bettelheim p at al… Comparison of the effects of tranexamic acid and aprotonin on blood loss and related variables in CPB. Journal of cardiovascular sciences..1994;108:1083-91

6) Murkin J M falter et al.. High dose tranexamic acid in relation to seizures in cardiac surgery patients. Anaesthesia anal..2010; 350:10

7) Gordon van basten et al Tranexamic acid in reducing bleeding in surgical patients. Journal of cardiothoracic and vascular sciences..2004;143:220-9.

8) Armando maradonna et al.. Tranexamic acid and aprotonin ..comparative clinical trial. Annals of thoracic surgery. 2009;321:437.

ANNEXURE ONE

- ABBREVIATIONS
- ASD--- ATRIAL SEPTAL DEFECT
- MVR—MITRAL VALVE REPLACEMENT
- AVR—AORTIC VALVE REPLACEMENT
- DVR---DOUBLE VALVE REPLACEMENT
- CABG-CORONARY BYPASS GRAFT BYPASS SURGERY
- TX GROUP- TRANEXAMIC ACID GROUP
- RHD—RHEUMATIC HEART DISEASE
- AS----AORTIC STENOSIS
- MS ---MITRAL STENOSIS
- CT—CLOTTING TIME
- PL—PLATELET COUNT
- Aptt—ACTIVATED PARTIAL THROMBO PLASTIN TIME

ANNEXURE TWO

PROFORMA FOR THE DATA COLLECTION FROM EACH PATIENT

NAME	:
AGE	:
SEX	:
IP NO	:
DOA	:
DOS	:
DIAGNOSIS	:
SURGERY	:
PRE OP INVESTIGATIONS	:
POST OP INVESTIGATIONS	:
TOTAL CPB TIME	:
TOTAL CROSS CLAMP	:
NO OF C P	:
BLOOD LOSS(DRAINS) AT 6 HOURS POST OP	:
DRAINSAT 12 HOURS POST OP	:
AT 24 HOURS POST OP	:
NEED FOR RED CELL TRANSFUSIONS(NO)	:
OTHER BLOOD PRODUCTS USED	:
THROMBOEMBOLIC EVENTS IF ANY	:
POST OP COMPLICATIONS IF ANY	:

DATE : Signature of investigator

PLACE :

ANNEXURE THREE

Bµõ#a] uPÁÀ uõÒ

C¸u¯ AÖøÁ]QaøŒ öŒ#²® @£õx C¸u¯zvß C¯UP® {Özu¨£mkAuß µzu Kmh•® uøhöŒ#¯¨£kQÓx. A¢u Œ©¯zvÀC¸u¯zøu £õxPõUP]» ÁÈ •øÓPÒ EÒÍÚ. AÖøÁ]QaøŒUS¨¤ß £»¸US Cµzu® EøÓ²® ußø© SøÓ¢xCµzu® @Œu©øhQÓx. C¢u B#Âß@£õxCøuSøÓ¨£uØSiµÚUŒªU B]mGßÝ® ©¸¢x E£@¯õQUP¨£k®.

}[PÒ C¢uBµõ#a]°À £[@PØP |õ[PÒ Â¸®¦Q@Óõ®. AuÚõÀ @|õ°ßB#ÁÔUøP@¯õAÀ»x]QaøŒ@¯õ £õv¨¦US HØ£hõx Gß£øu²® öu›ÂzxUöPõÒQ@Óõ®.

•iÄPøÍ AÀ»x P¸zxUPøÍ öÁÎ°k® ö£õÊ@uõ AÀ»x Bµõ#a]°ß ö£õÊ@uõ u[PÍx ö£¯øµ@¯õ AÀ»x Aøh¯õÍ[PøÍ@¯õ öÁÎ°h©õm@hõ® Gß£øu²® öu›ÂzxU öPÒQ@Óõ®.

C¢uBµõ#a]°À £[@PØ£x u[PÐøh¯ Â¸¨£zvß @£›À uõß C¸UQÓx. @©¾® }[PÒ G¢@|µ•® C¢u Bµõ#a]°À C¸¢x ¤ßÁõ[P»õ® Gß£øu²® öu›ÂzxUöPõÒQ@Óõ®.

C¢u £›@ŒõuøÚ°ß •iÄPøÍ Bµõ#a]°ß @£õx AÀ»x Bµõ#a]ß •iÂß@£õx u[PÐUS AÔÂ¨@£õ® Gß£øu²® öu›ÂzxU öPõÒQ@Óõ®.

Bµõ#a]¯õÍº øPö¯õ¨£® £[@PØ£õÍº øPö¯õ¨£®

@uv :

ANNEXURE FOUR

Bµõ#a] J¨¦uÀPiu®

Bµõ#a] uø»¨¦ : ""C¸u¯ AÖøÁ]QaøŒUS¨¤ß HØ£k® Cµzu® CÇ¨ø£ SøÓUPEuÄ® iµÚUŒªU B]m".

ö£¯º	:	@uv	:
Á¯x	:	EÒ@|õ¯õÎGs	:
£õÀ	:	Bµõ#a] @ŒºUøP Gs.	:

B#Ä öŒ#²®

{ÖÁÚzvß ö£¯º : öŒßøÚ ©¸zxÁUPÀ¿›

C¢uBµõ#a]°ß ÂÁµ[PÐ® @|õUP[PÐ® •Êø©¯õP GÚUS öuÎÁõP ÂÍUP¨£mhx.

GÚUS ÂÍUP¨£mhÂå¯[PøÍ |õß ¦›¢x öPõsk |õßGÚx Œ®©uzøuöu›ÂUQ@Óß.

C¢uBµõ#a]°À ¤Ó›ß {º£¢uªßÔGßöŒõ¢u Â¸¨£zvß @£›À uõß £[S ö£ÖQ@Óß ©ØÖ® |õßC¢u Bµõ#aŒ°¼¸¢x G¢@|µ•® ¤ßÁõ[P»õ® Gß£øu²® AuÚõÀG¢u £õv¨¦® HØ£hõx Gß£øu²® |õß ¦›¢x öPõs@hß.

|õßC¢uBµõ#a] SÔzuuPÁÀuõøÍö£ØÖUöPõs@hß.

|õßGßÝøh¯ ”¯ {øÚÄhß ©ØÖ® •Ê ”u¢vµzxhßC¢u ©¸zxÁBµõ#a]°À GßøÚ @ŒºzxöPõÒÍ Œ®©vUQ@Óß.

GßÝøh¯ µzu £›@ŒõuøÚ •iÄPøÍBµõ#a] öŒ#xöPõÒÍ Œ®©vUQ@Óß.

C¢u £›@ŒõuøÚ°ÚõÀ GÚUS G¢uÂu©õÚ £UP ÂøÍÄP@ÍõAÀ»x ¤ß ÂøÍÄP@ÍõHØ£hõx Gß£øu²® ©¸zxÁº ‰»® öu›¢x öPõs@hß.

Bµõ#a]¯õÍº øPö¯õ¨£® £[@PØ£õÍº øPö¯õ¨£®

@uv :

ANNEXURE FIVE

Sl.No.	Name	Age/ Sex	IP No.	Diagnosis	Surgery	Total CPB Time	No of CP	Total Cross Clamp Time	Pre of OP platelet, CT, BT	Post of Blood Loss	6 Hrs	12 Hrs	24 Hrs	PC Transfusion	Thromboembolic Events

INSTITUTIONAL ETHICS COMMITTEE

MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No. ECR/270/Inst./TN/2013
Telephone No: 044 25305301
Fax: 044-25363970

CERTIFICATE OF APPROVAL

To:
Dr. Prem anand J,
MCh cardiothoracic surgery post graduate,
Madras Medical College, Chennai-3.

Dear **Dr. Prem anand ,**

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled **"USEFULNESS OF TRANEXAMIC ACID IN REDUCING POST OPERATIVE BLEEDING IN PATIENTS UNDERGOING CARDIAC SURGERY "** No.11122013

The following members of Ethics Committee were present in the meeting held on 11.12.13 conducted at Madras Medical College, Chennai-3.

1. Dr. G. Sivakumar, MS FICS FAIS	-- Chairperson
2. Prof. B. Kalaiselvi, MD Vice Principal, MMC, Ch-3	-- Member Secretary
3. Prof. Ramadevi, Director i/c Inst. Of Biochemistry, Chennai.	-- Member
4. Prof. P. Karkuzhali, MD for Dr. V. Ramamoorthy Prof. Inst. Of Pathology, MMC, Ch-3	-- Member
5. Thiru. S. Govindasamy, BA,BL	-- Lawyer
6. Tmt. Arnold Saulina, MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd /Chairman & Other Members

The Institutional Ethics Committed expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patient's information /informed consent and asks to be provided a copy of the final report.

27-12-13

sdMember Secretary, Ethics Committee

turnitin

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	18111003 . M.ch. Cardio Thoracic Surgery PREM ANAND J . JOHN
Assignment title:	Medical
Submission title:	Usefulness of tranexamic acid in reducing post operative bleeding in patients undergoing cardiac surgery
File name:	PREM_ANAND_THESES_FINAL.docx
File size:	416.81K
Page count:	63
Word count:	4,755
Character count:	26,436
Submission date:	25-Mar-2014 04:12PM
Submission ID:	409405658

DISSERTATION ON

USEFULLNESS OF TRANEXAMIC ACID IN REDUCING POST OPERATIVE BLEEDING IN PATIENTS UNDERGOING CARDIAC SURGERY

submitted in partial fulfillment of requirements of

M.CH DEGREE EXAMINATION

BRANCH

CARDIO VASCULAR AND THORACIC SURGERY

MADRAS MEDICAL COLLEGE AND

RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL

CHENNAI – 600 003.

AUGUST 2014